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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/142,660	12/23/98	HINTSCHE	R 99953/11*

EXAMINER

SISSON,B

ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/142,660	Applicant(s) HINTSCHE ET AL.	
	Examiner Bradley L Sisson	Art Unit 1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 and 28 August 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-55 and 58-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-55 and 58-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *08 June 2001* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *26 & 30* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 01 August 2001 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/142,660 is acceptable and a CPA has been established. An action on the CPA follows.

Drawings

2. The proposed drawing correction and/or the proposed substitute sheet of drawings filed on 08 June 2000 have been approved by the examiner.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 21-55 and 58-61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for coating of an electrode with SH-biotin and detection/measurement of β-galactosidase-streptavidin wherein said β-galactosidase-streptavidin binds to the immobilized biotin and is subsequently detected by the action of β-galactosidase on ρ-aminophenol, does not reasonably provide enablement for the detection of any molecule complex in any diluent, be it in a purified state or not, and where the ultra-microelectrode array

is fashioned of any material and is operated under any strength of electric field, any amplitude, and any frequency. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *In re Wands*, 8 USPQ2d 1400 (CAFC 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Quantity of Experimentation Necessary

The amount of experimentation is great, on the order of many man-years with little if any reasonable expectation of success.

The Amount of Direction or Guidance Provided and The Presence or Absence of Working Examples

The specification has been found to provide but one example where any molecule was detected and that was for the presence of β-galactosidase-streptavidin. In accordance with the example provided at pages 13-14 of the specification, SH-Biotin was first coated onto a gold electrode that had a width of 1 μm and an electrode spacing of 0.7 μm. The modified electrode

was then dipped for 2 hours in a 50 U/ml solution of β-galactosidase-streptavidin and subsequently rinsed for 10 minutes in 0.1 mol/ml Na buffer solution.

As set forth at page 14, a Nyquist plot for a potential of 50 mV, amplitude of 10 mV and a frequency range of between $2x10^{-13}$ Hz and $1X10^{6}$ Hz, measured as two-pole impedance.

The specification does not set forth the conditions required to accurately detect any other molecule or molecule complex in any diluent under any set of conditions. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

> " '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').
>
> *****
>
> "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.
> "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a

> failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research.

Claim 23 requires measurement to be made via impedance spectroscopy. However, the specification does not set forth a repeatable procedure whereby this is to be conducted. The specification does not enable the application of "a direct-current component", nor the oxidation or reduction of an electrically active molecule.

Claims 28-30, while limiting of claim 21, clearly indicate that the claims are to encompass the induction of any and all possible electrochemical reactions. The specification has not set forth a sufficient number of members of the genus of electrochemical reactions so to enable the genus. While the specification need not set forth an example of each and every possible permutation encompassed by the claims, the specification does need to fully enable the complete scope of the invention. Additionally, greater levels of disclosure are required where the invention is drawn to an inherently unpredictable area, such as the chemical and physiological arts; see *In re Fisher* 166 USPQ 18, 24 (CCPA 1970) and *In re Shokal*, 113 USPQ 283 (CCPA 1957). Similarly, the specification does not set forth a repeatable procedure where the molecule to be detected is an antibody (claim 40) or an antigen (claim 41), nor for when the first and or second molecules comprise polynucleotides (claims 42-44). The specification has not been found to set forth a repeatable procedure whereby one of skill in the art would be able to synthesize and use an electrode fashioned of a material other than gold. The limited guidance has not been found to be sufficient to enable the full scope of the claimed invention.

The Nature of the Invention

The invention relates to the detection of virtually any molecule or molecular complex, be it in a purified or heterogeneous mixture, and regardless of concentration. The claimed method employs an alternating electrical current and the skilled artisan is to measure changes in current or in electrical potential between electrode structures which are to be interpreted as being indicative of a molecule or molecular complex.

The State of the Prior Art

The state of the prior art in this area is relatively undeveloped, especially when one is attempting to detect any type of molecule or molecular complex, be it in a purified or heterogeneous mixture of varying concentrations, buffers, temperatures, etc.

The Relative Skill of Those in the Art

The relative skill of those in the art most closely related to the claimed invention is high, on par with those who hold a Ph.D. in biochemistry and have a firm grounding on electrical chemistries.

Breadth of the claims

The claims have sufficient breadth of scope so to encompass the detection and identification of one or more molecules at a time. The claims also have sufficient breadth of scope so to encompass the use of electrodes that are in contact with one another as well as those that are separated by a subatomic distance. Support for this interpretation is based in part on the

limitation whereby the electrodes are to be spaced "less than 3 μm" apart (claims 21-55 and 58-60) or be spaced "less than 1 μm" apart (claim 61).

Response to Arguments

Applicant's representative directs attention to the declarations filed under 37 CFR 1.132 by a) Dr. Rainer Hintsche and Dr. Manfred Paeschke; and b) Dr. Rainer Hintsche.

Upon review of the declaration of Dr. Rainer Hintsche and Dr. Manfred Paeschke it is noted that the declarants are also the inventors and as such have a vested interested in the outcome of the examination of the subject application. The declaration is found to contain the opinion of both with assertions that one of ordinary skill in the art could readily adapt prior art methods so to enable the claimed invention. Attention is directed to non-patent literature as well as to foreign patents and to two US patents.

The above arguments have not been found persuasive towards the withdrawal of the rejection for as stated in the decision of *Genentech*:

> "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research.

Declarants have not shown how the specification fully enables the full scope of the claims without having to resort to undue experimentation. The aspect of world patent documents or PCT applications being published is immaterial to the present issue of enablement as they are not US patents. Even in the case of US Patents 5.572,256 and 5,653,939, such publications do not have any bearing on the present application as each application is considered on its own merits. Accordingly, the opinion declaration of Dr. Rainer Hintsche and Dr. Manfred Paeschke has not been found persuasive towards the withdrawal of the rejection.

The second declaration presented is also that of co-inventor Dr. Rainer Hintsche and as such has a vested interest in the prosecution of the subject application. The Declaration presents experimental examples with detailed explanation as to how the four examples were conducted. Said examples are found to contain bibliographical reference to numerous non-patent publications were relied upon in practicing the examples. A review of the disclosure of the subject application does not find that these prior art publications were relied upon for enablement. The examples presented in the declaration so to demonstrate enablement are not commensurate in scope with the disclosure of the subject application. Accordingly, and in the absence of convincing evidence to the contrary, the declaration has not been found to be persuasive towards the withdrawal of the rejection.

Conclusion

5. This is a CPA of applicant's earlier Application No. 09/142,660. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier

application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

B. L. Sisson

Bradley L Sisson
Primary Examiner
Art Unit 1655

bls
September 17, 2001